American Journal of Hematology 58:246–247 (1998)

Mesenteric Artery Thrombosis: A Case Report of Combined Protein S and Protein C Deficiency

Kristen A. Atkins* and James L. Zehnder
UCSF-Stanford Health Care, Stanford, California

Individuals with more than one defect in natural coagulant/anticoagulant systems have been postulated to be at an increased risk for thrombotic events. We report a case of combined protein S and C deficiency in a young woman, which resulted in fatal arterial mesenteric thrombosis. The role of coagulation defects in arterial thrombosis is discussed. Am. J. Hematol. 58:246–247, 1998. © 1998 Wiley-Liss, Inc.

Key words: protein S; protein C; combined deficiencies; arterial thrombosis; mesenteric thrombosis

INTRODUCTION

Deficiency in the vitamin K dependent proteins, protein S and protein C, can be acquired or inherited and presents with a range of clotting problems from asymptomatic to recurrent, sometimes lethal, thrombosis. Protein S enhances the activity of activated protein C in the degradation of clotting factors Va and VIIIa. Congenital heterozygous protein S and C deficiency are both associated with increased propensity for thrombosis, each accounting for 5–10% of patients presenting with deep venous thrombosis and pulmonary emboli [1]. Although arterial thrombosis is unusual in protein C deficiency, protein S deficiency has been reported as a cause for arterial thrombosis in people under the age of 45 years [2]. We now report a previously healthy middle-aged woman with a bowel infarct and combined deficiency in protein C and protein S.

CASE REPORT

A 46-year-old woman, with no prior or family history of thrombosis, had persistent vague abdominal pain, unresolved by cholecystectomy. On 9/11/96 she was admitted to a hospital with severe abdominal pain.

An exploratory laparotomy revealed two segments of ischemic bowel requiring a partial small bowel resection. She was transferred to our institution where an angiogram showed occlusion of the proximal superior mesenteric artery. The patient underwent revascularization utilizing the saphenous vein, as well as a second small bowel resection for additional ischemic bowel.

Prior to heparin therapy, coagulation studies were drawn (results in Table I). After surgery the patient remained ventilator dependent. During the hospital course, several abdominal abscesses were drained and multiple positive cultures were obtained. By 10/25 the patient developed renal insufficiency and hepatic failure. On 11/13, an episode of ventricular tachycardia resulted in severe neurologic damage. After conferring with the family, all life support measures were withdrawn and the patient expired on 11/13/96. Permission for an unrestricted autopsy was granted.

Autopsy Findings

The saphenous vein graft was patent, bypassing a mildly atherosclerotic thrombosed native artery. The proximal aspects of the other abdominal arteries were patent with focal fatty streaking. The arterial courses were not completely dissected secondary to extensive adhesions. No thrombus was found in the leg veins.

The liver weighed 2,100 g (normal 1,400 g) and was diffusely necrotic. Histologically the liver contained rare viable hepatocytes and a mild neutrophil infiltrate.

The coronary, pulmonary, and cerebral arteries were patent.

*Correspondence to: Kristen Atkins, M.D., UCSF-Stanford Health Care, Room H2110, Stanford, CA 94305. E-mail: katkins@pathology.stanford.edu

Received for publication 29 January 1998; Accepted 18 March 1998

TABLE I. Coagulation Studies Showing Type I Protein S Deficiency and Type II Protein C Deficiency*

PT/INR	13.1/1.2
PTT	31.1
Protein C (%)	
Activity	67 (83–143)
Antigenic level	99 (69–129)
Protein S (%)	
Activity	21 (65–166)
Antigen Level	36 (58–146)
ATIII (%)	79 (86–120)
Factor V Leiden	Normal
Anticardiolipin Ab	Negative
Homocysteine	4 (4–20)

*PT, prothrombin time; PTT, partial thromboplastin time.

DISCUSSION

Acute mesenteric ischemia is typically the result of thrombosis, embolism, or nonocclusive ischemia [3]. Mesenteric artery thrombosis is an unusual presentation for a young female. A Finnish study found that thrombosis in visceral arteries is the most common cause of acute mesenteric ischemia, usually attributable to atherosclerosis. In their patient population, however, 67% were over the age of 80 years and only 6% were less than 40 years [4]. Although this patient did have risk factors for atherosclerosis, including a smoking history and hypertension, her age of onset and location are unusual. When the mesenteric venous system is effected, many times a hypercoagulable state is identified [5]. Little is in the literature regarding arterial occlusion and protein deficiencies.

Although protein S and C deficiencies each account for 5–10% of hereditary thrombophilic states, most of these are venous in origin. Arterial thrombosis associated with natural anticoagulant deficiency is uncommon but has been reported in association with protein S deficiency. Other reports have implicated factor V Leiden and homocysteinemia, neither of which were present in this patient.

Recently, it has become apparent that individuals with more than one compromising factor in the homeostatic mechanism have an increased risk over those with a single risk factor. It appears likely that the risk of a thrombotic event is related to the number of risk factors, genetic or acquired, which are present simultaneously. Numerous studies have now documented the increased risk of individuals with more than one anomaly in the homeostatic mechanism.

Combined protein S and C defects are rare and have been documented in association with strokes in young adults [6]. Koller et al. [6] postulated that combined disorders may increase the risk of arterial thrombotic disorders, especially ischemic strokes, in young adults.

Protein S and C deficiency can be divided into two categories. Type I is defined as a decrease in total concentration, antigenic level, and activity. Type II is a qualitative defect with normal total and antigen levels but a decreased activity. The patient's coagulation profile (Table I) shows both type I proteins S deficiency (decreased total and activity) and type II protein C deficiency (normal total and a decreased activity). The slightly prolonged PT may be secondary to hepatic synthetic defect, exacerbating the underlying protein S and protein C deficiencies. However, the normal protein C antigen level argues against a global hepatic synthetic defect.

Although most people with protein S or C deficiency have no precipitating factor initiating the thrombus, 30–40% do have triggering events such as sepsis, pregnancy, immobility, or vascular conditions such as atherosclerosis [7,8]. This patient had focal atherosclerosis in the mesenteric arteries. Currently, mesenteric ischemia with resultant bowel necrosis holds a mortality rate between 80–95%, typically, as in this patient, secondary to multiorgan system failure and sepsis [3]. Earlier detection and aggressive antithrombotic therapy in individuals with hypercoagulable states may help improve these statistics. Hereditary thrombophilia should be suspected in young people with unusual thrombotic presentations even in the presence of atherosclerosis. This case further validates the hypothesis that multiple defects in the anticoagulant system can lead to increased thrombotic risk and severity of thrombosis.

REFERENCES

1. Bick R, Pegram M: Syndromes of hypercoagulability and thrombosis: A review. Semin Thromb Hemost 20:109–132, 1994.
2. Allart C, Aronson D, Ruys T, Rosendaal F, Bockel J, Bertina R, Briet E: Hereditary protein S deficiency in young adults with arterial occlusive disease. Thromb Hemost 64:206–210, 1990.
3. Schneider T, Longo W, Ure T, Veranara A: Mesenteric ischemia. Dis Colon Rectum 37:1163–1174, 1994.
4. Jarvinen O, Laurekka J, Sisto T, Salenius J, Tarkka M: Atherosclerosis of visceral arteries. Vasa 24:9–14, 1995.
5. Zigrossi P, Campanini M, Bordin G, Arceci G, Gamba P, Gnemmi P, Monteverde A: Portal and mesenteric thrombosis in protein S Deficiency. Am J Gastroenterol 91:163–165, 1996.
6. Koller H, Stoll G, Sitzer M, Burk M, Schottler H, Freund H: Deficiency of both protein C and protein S in a family with ischemic strokes in young adults. Neurology 44:1238–1240, 1994.
7. Girolami A, Simioni P, Scarano L, Girolami B: Venous and arterial thrombophilia. Hematologica 82:96–100, 1997.
8. Gouault-Heilmann M, Leroy-Matheron C, Levent M: Inherited protein S deficiency: Clinical manifestations and laboratory findings. Thromb Res 76:269–279, 1994.